Tissue Engineered Human Hair: Preliminary Clinical Results

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INTRODUCTION

One of the highest goals of tissue engineering is to create fully functional human organs that are in short supply for transplantation. The hair follicle is a complex, albeit microscopic, organ that is in short supply from the viewpoint of the hair restoration surgeon. Although it is well established that cultured dermal papilla cells have the capacity to induce the formation of new hair follicles,[1,2] this knowledge heretofore has not been successfully exploited for the purpose of developing an improved method of hair restoration.

In the present study, a preliminary human clinical investigation was conducted to examine potentially critical variables as a first step in developing a procedure for hair restoration using the basic principles of tissue engineering.[3]

MATERIALS AND METHODS

Eight men scheduled to undergo elective surgery for hair restoration were enrolled in this IRB approved study upon obtaining their informed consent. During surgery a slightly larger than required strip of donor site scalp was excised and the excess tissue taken to the laboratory where dermal papillae (DP) were dissected from the follicles and cultured as described previously.[4] The cultured DP cells were implanted back into the same subjects from whom they were harvested in four sites behind the ear. Each site was marked with a small tattoo spot of carbon particles and biopsied with a 3.5 mm punch 6 to 12 weeks post-implantation. Biopsy specimens were processed for paraffin embedding, stained with H&E, and 4 micron slices were evaluated by a board certified dermatopathologist (A.R.S.).

The first 4 subjects (Group A) received injections of various numbers of cells suspended in minimum essential media (MEM) with and without Pluronic™ F-127 (BASF Corp.), a gel-forming surfactant that has shown utility in a previous study designed to create tissue engineered elastic cartilage.[5] A custom engineered injection device was utilized to control the depth and angle of intra-dermal injection and allowed simultaneous injection and needle withdrawal from the skin to deposit the cells in the needle track. The next 4 subjects (Group B) received cells seeded onto two different types of porous scaffolds comprised of poly(*d,l*-lactide-*co*-50%-glycolide) (PLGA) (Resomer™ RG504, Boehringer Ingelheim, Germany) and crosslinked porcine skin gelatin (Gelfoam™, Pharmacia-Upjohn). These scaffolds were implanted by different methods: B-1&2 by incision and B-3&4 by "bleb incision", a technique in which the epidermis is temporarily separated from the dermis by injection of hyaluronic acid (Healon™, sodium hyaluonate, Pharmacia-Upjohn) prior to incision. Hyaluronic acid (HA) also was used to modify the surface of Gelfoam™ covalently using a water-soluble condensing agent[6] in one experimental group, imparting greater hydrophilicity and improved physical integrity to the scaffold.

RESULTS AND DISCUSSION

The number of cells suspended in the formulations injected in Group A subjects among the 16 injection sites varied from zero (control) to 7.6 million cells per milliliter. Although exactly 50 micro-liters of fluid was expressed from the syringe during each injection, it was not possible to confirm the actual number of cells retained in the skin because a portion of the fluid extruded back out of the sites due to over pressurization. Each site was covered with Tegaderm™ transparent film (3M) to prevent any further loss of fluid post-injection. None of the injection sites in Group A subjects showed evidence of new hair growth upon inspection prior to biopsy. Histological findings were normal for several sections that were examined. Although not all biopsy specimens were processed beyond paraffin embedding, we hypothesize that the suspension of single cells was insufficient to induce follicle neogenesis because the injected cells lacked the conditions required to clump together and therefore were resorbed.

All sites in Group B subjects were implanted with scaffolds that possessed DP cells as clumps of cells, either by combining clumps of cells with the scaffold or allowing the cells to grow into and attach to the scaffold during *in vitro* cultivation. Of the 16 implantation sites, one showed unequivocal growth of 2 new hair shafts emerging from the skin, shown in Figure 1. Many other sites, examined histologically, revealed both normal and abnormal follicular structures that formed in juxtaposition with remnants of degraded scaffold materials and residual inflammatory cells.

A continuation of this study is being planned to replicate the induction of hair-producing follicles and further define implant characteristics required for use in hair restoration.

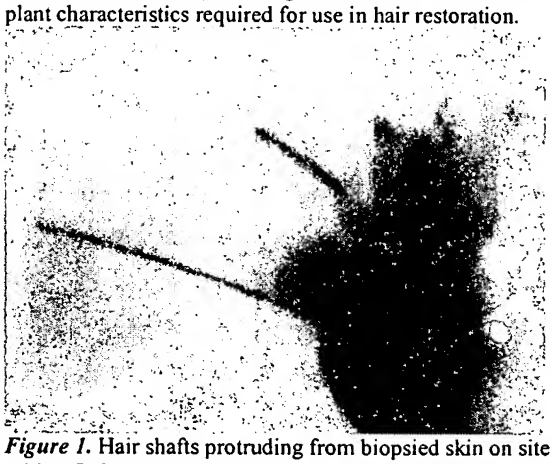

Figure 1. Hair shafts protruding from biopsied skin on site #2 of subject B-3 at 8 weeks post implantation of DP cells cultured on HA-treated Gelfoam™. The distal ends were cut off by the biopsy punch.

CONCLUSION

We believe the results of this study to be the first documented clinical demonstration of follicle neogenesis and hair growth *via* implantation of DP cell-seeded bioabsorbable scaffolds into human skin.

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